

Non-targeted effects of ionising radiation (NOTE) – a new European Integrated project, 2006-2010

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The universality of the target theory of radiation-induced effects is challenged by observations on non-targeted effects such as bystander effects, genomic instability and adaptive response. Essential features of non-targeted effects are that they do not require direct nuclear exposure by radiation and they are particularly significant at low doses. This new evidence suggests a need for a new paradigm in radiation biology. The new paradigm should cover both the classical (targeted) and the non-targeted effects. New aspects include the role of cellular communication and tissue-level responses. A better understanding of non-targeted effects may have important consequences for health risk assessment and, consequently, on radiation protection. Non-targeted effects may contribute to the estimation of cancer risk from occupational, medical and environmental exposures. In particular, they may have implications for the applicability of the Linear-No-Threshold (LNT) model in extrapolating radiation risk data into the low-dose region. This also means that the adequacy of the concept of dose to estimate risk is challenged by these findings. Moreover, these effects may provide new mechanistic explanations for the development of non-cancer diseases. Further research is required to determine if these effects, typically measured in cell cultures, are applicable in tissue level, whole animals, and ultimately in humans.

The general objectives of the NOTE project are:

- to investigate the mechanisms of non-targeted effects, in particular, bystander effects, genomic instability and adaptive response;
- to investigate if and how non-targeted effects modulate the cancer risk in the low dose region, and whether they relate to protective or harmful functions;
- to investigate if ionising radiation can cause non-cancer diseases or beneficial effects at low and intermediate doses;
- to investigate individual susceptibility and other factors modifying non-targeted responses;
- to assess the relevance of non-targeted effects for radiation protection and to set the scientific basis for a modern, more realistic, radiation safety system;
- to contribute to the conceptualisation of a new paradigm in radiation biology that would cover both the classical direct (DNA-targeted) and non-targeted (indirect) effects.

The NOTE brings together 19 major European and Canadian groups involved in the discovery, characterisation and mechanistic investigation of non-targeted effects of ionising radiation in cellular, tissue and animal models (see Fig. 1).

The NOTE research activities are organised in six work packages (see Fig. 1). Four work packages (WPs 2-5) are problem-oriented, focussing on major questions relevant for the scientific basis of the system of radiation protection. The integration activities provided by WP6 strengthen the collaboration by supporting the access to infrastructures, mobility and training. WP7 provides dissemination and exploitation activities in the form of workshops and a public website. Managerial activities (WP1) ensure the organisation and structures for decision making, monitoring of progress, knowledge management and efficient flow of information and financing.

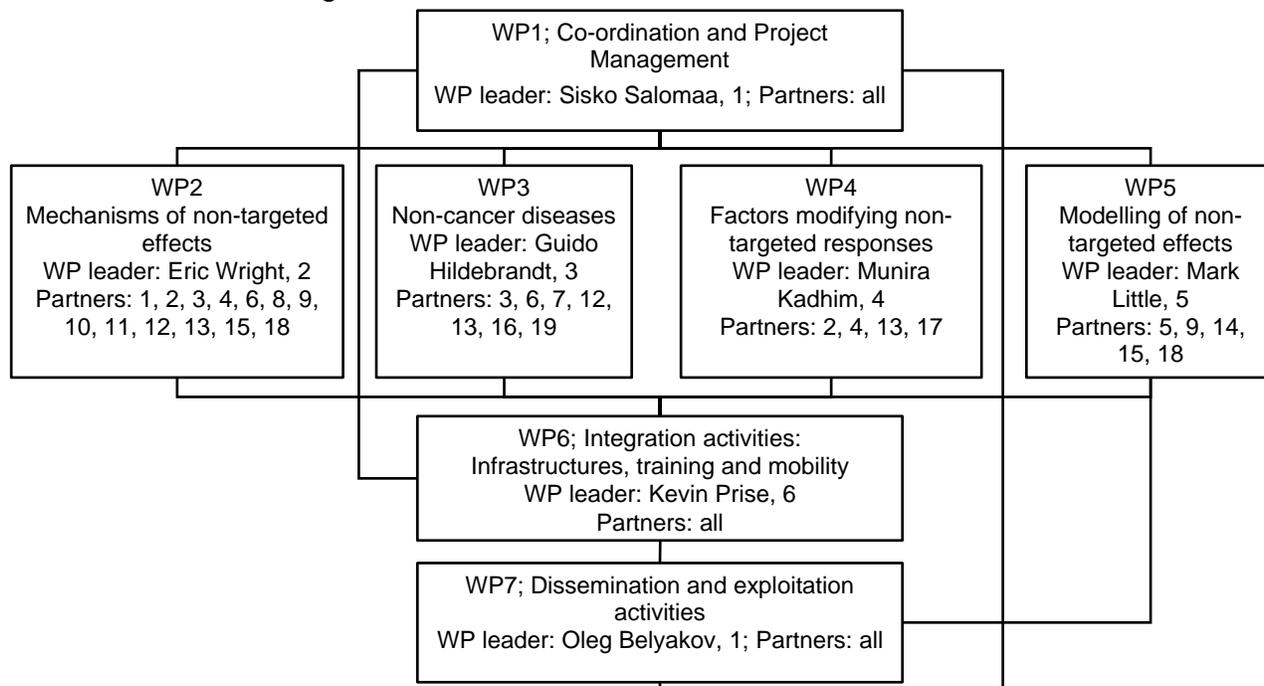


Figure 1. Structure of NOTE consortium. (1) Radiation and Nuclear Safety Authority, Finland; (2) University of Dundee, UK; (3) Leipzig University, Germany; (4) MRC Radiation and Genome Stability Unit, UK; (5) Imperial College, UK; (6) Gray Cancer Institute, UK; (7) Belgian Nuclear Research Centre, Belgium; (8) Dublin Institute of Technology, Ireland; (9) National Institute of Health, Italy; (10) University of Leicester, UK; (11) McMaster University, Canada; (12) Atomic Energy of Canada Limited, Canada; (13) National Research Institute for Radiobiology and Radiohygiene, Hungary; (14) National Research Centre for Environment and Health, Germany; (15) University of Pavia, Italy; (16) University of Erlangen-Nuremberg, Germany; (17) University of Duisburg-Essen, Germany; (18) Norwegian Radium Hospital, Norway; (19) Ottawa Heart Institute Research Corporation, Canada.

Coordinator of the NOTE project is Prof. Sisko Salomaa, STUK - Radiation and Nuclear Safety Authority, Helsinki, Finland.

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Please visit the project website <http://www.note-ip.org> to obtain more information or contact us by e-mail note@stuk.fi.